

Amendments to the Specification:

Please replace the paragraph beginning at page 5, line 17, with the following redlined paragraph.

Figure 3 is a sequence alignment showing sequence similarity between DSP-2 (SEQ ID NO:17) and other MAP-kinase phosphatases: PYST1 (SEQ ID NO:10); MKP-7 (SEQ ID NO:11); PAC1 (SEQ ID NO:12); MKP-1 (SEQ ID NO:13); MKP-4 (SEQ ID NO:14); MKP-5 (SEQ ID NO:15); and hVH5 (SEQ ID NO:16).

Please replace the paragraph beginning at page 9, line 3, with the following redlined paragraph.

DSP-2 polynucleotides may comprise a native sequence (*i.e.*, an endogenous DSP-2 sequence or a portion or splice variant thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the activity of the encoded polypeptide is not substantially diminished, as described above. The effect on the activity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native DSP-2 or a portion thereof. The percent identity may be readily determined by comparing sequences using computer algorithms well known to those having ordinary skill in the art, such as Align or the BLAST algorithm (Altschul, *J. Mol. Biol.* 219:555-565, 1991; Henikoff and Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915-10919, 1992), which is available at the NCBI website (<http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST>). Default parameters may be used. Certain variants are substantially homologous to a native gene. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA or RNA sequence encoding a native DSP-2 (or a complementary sequence). Suitable moderately stringent conditions include, for example, prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0

mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, for 1-16 hours (*e.g.*, overnight); followed by washing once or twice at up to 65°C for 20-40 minutes with one or more each of 2X, 0.5X and 0.2X SSC containing 0.05-0.1% SDS. For additional stringency, conditions may include a wash in 0.1X SSC and 0.1% SDS at 50-60 °C for 15-40 minutes. As known to those having ordinary skill in the art, variations in stringency of hybridization conditions may be achieved by altering the time, temperature and/or concentration of the solutions used for prehybridization, hybridization and wash steps, and suitable conditions may also depend in part on the particular nucleotide sequences of the probe used, and of the blotted, proband nucleic acid sample. Accordingly, it will be appreciated that suitably stringent conditions can be readily selected without undue experimentation where a desired selectivity of the probe is identified, based on its ability to hybridize to one or more certain proband sequences while not hybridizing to certain other proband sequences.

Please replace the paragraph beginning at page 11, line 12, with the following redlined paragraph.

A cDNA sequence encoding DSP-2 is provided in Figure 1 (SEQ ID NO:1), and the predicted amino acid sequence is provided in Figure 2 (SEQ ID NO:2). The DSP-2 active site LHCAAGVSRS (SEQ ID NO:3), is ~~encoded by nucleotide bases located at nucleotide-amino~~ acid positions 102 through 111 of SEQ ID NO:1 SEQ ID NO:2. Sequence information immediately adjacent to this site was used to design 5' and 3' RACE reactions with human thymus cDNA to identify a protein of 188 amino acids that displays a higher abundance in tissue of the immune system. This protein is referred to as dual specificity phosphatase-2, or DSP-2. DSP-2 shows significant homology to other MAP-kinase phosphatases, as shown by the sequence comparison presented in Figure 3.

Please replace the paragraph beginning at page 30, line 7, with the following redlined paragraph.

A conserved sequence motif surrounding the active site domain of dual-specificity phosphatases was identified as follows: Dual specificity phosphatases belong to the larger family of protein tyrosine phosphatases (PTPs) that share a conserved catalytic domain containing a cysteine residue situated N-terminal to a stretch of five variable amino acids followed by an arginine residue (Fauman et al., *Trends In Bioch. Sci.* 21:413-417, 1996). DSPs typically contain a PTP active site motif but lack sequence homology to PTPs in other regions (Jia, *Biochem. and Cell Biol.* 75:17-26, 1997). There is, however, no reported consensus sequence that is conserved among DSPs, nor is a consensus region apparent from examination of the known DSP sequences such as those referred to above. To derive a longer consensus DSP amino acid sequence motif that would be useful for the identification of new DSP family members, multiple known human dual-specificity phosphatases sequences were aligned and compared. An alignment of eight amino acid sequences derived from eight human DSPs having MAP-kinase phosphatase activity yielded a conserved homology region consisting of a 23-amino acid peptide sequence containing the PTP active site signature motif. Thus, a candidate peptide having the sequence:

GRVLVHCQAGISRSGTNILAYLM

SEQ ID NO:4

was used to search the Expressed Sequence Tag database (Nat. Center for Biol. Information, ~~www.ncbi.nlm.nih.gov/dbEST~~). The search employed an algorithm (tblastn) capable of reverse translation of the candidate peptide with iterations allowing for genetic code degeneracy within default parameters. The search results identified the EST AA915932, as well as AA926744, AA527292, AI215158 and AA356476, as candidate MAP-kinase phosphatases. The ESTs did not include a complete coding region of an expressed gene such as a gene encoding a DSP-2 having MAP-kinase phosphatase activity, nor were the sense strand and open reading frame identified.

Please replace the paragraph beginning at page 31, line 15, with the following redlined paragraph.

A cDNA (Figure 1; SEQ ID NO:1) encoding a protein of 188 amino acids (Figure 2; SEQ ID NO:2) was identified as DSP-2. This sequence has significant homology to other MAP-kinase phosphatases (Figure 3). The identified cDNA contains the 564 base pair coding region, as well as associated 5' and 3' untranslated sequences. The active site domain for DSP-2 was localized to the region ~~encoded by nucleotides beginning at position 102 of SEQ ID NO:1~~ SEQ ID NO:2.